



HOW TO PRESCRIBE FURAZOLIDONE TO YOUR PATIENT

Please note that this product can only be prescribed under the TGA's 'Special Access Scheme' (SAS). Information and forms for this scheme are available online at www.health.gov.au/tga/docs/html/sasinfo.htm or by calling (02) 6232 8111.

Should you wish to prescribe Furasian® to a patient please follow the procedure outlined below.

1. Complete the "TGA-Category B Special Access Scheme" proforma No: 2950 (0105). Pro formas are available from the TGA web site or by calling (02) 6232 8111.
2. Fax the completed pro forma to the TGA (02) 6232 8112 (Phone: 02 6232 8111). Address it "For the Attention of The Medical Officer, SAS, Drug Safety & Evaluation Branch, TGA".
3. When TGA approval is received, fax the following to Tri-Med:
 - a. Copy of Application form
 - b. Copy of the Approved Notification received from the TGA
 - c. Order & Payment form

Once payment is received, TRI-MED will ship the prescription medicine to the prescribing medical practitioner (or the patient - if directed by the practitioner).

Please Note:

Generally, the Commonwealth does not subsidise (through Pharmaceutical Benefits Scheme - PBS) the cost of unregistered products such as Furasian® (Furazolidone). Questions about the PBS should be addressed to the PBS Telephone Information Line 1800 020 613.

Applicant and/or the patient may wish to check with TRI-MED as to the cost of the medicines involved prior to Step 3.

<u>CAT. NO.</u>	<u>DESCRIPTION DOSE</u>	<u>QUANTITY</u>	<u>RRP</u>
FUR0001	Furasian® 100 mg each tab.	1 Bottle (50 Tablets)	On application
FUR0014	Furasian® 100 mg each tab. (7 Day Course)	1 Bottle (14 Tablets)	On application

For further information regarding Furasian, please contact TRI-MED on Freecall 1800 08 05 07, or by email and Web site as listed below.

This price list supersedes all previous price lists.

TRI-MED Distributors reserve the right to review pricing if currency fluctuations varies by 5% or more (GMO/Mar04)



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PLEASE USE BLACK PEN, PRINT CLEARLY AND COMPLETE ALL SECTIONS

Patient details

Patient details (initials, ID or URN, DOB, Sex)	
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Diagnosis		Previous SAS No.	
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Clinical justification for use of product <i>Include appraisal of seriousness of patient's condition; detail previous treatments and expected benefits from use of the product</i>	H. pylori infection refractory to Losec Hp7
	Furazolidone treatment has potential for eradicating the above infection

Product details *Attach efficacy and safety data to support proposed use of the product and details of intended monitoring regime. *Complete for medicines only.*

Active* ingredient	Furazolidone	Trade name /Device name	Furasian
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Company/supplier	TRI-MED Distributors Pty Ltd
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Dose form*	100 mg tablet	Route of administration*	Oral
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Dosage*	100mg four times a day	Duration of treatment	14 days
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Prescribing doctor details

Name	<i>Initial Surname</i>	Hospital	
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Postal address		Department	
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		Phone	
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	<i>Postcode</i>	Fax number	
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Signature	
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INFORMATION ON FURAZOLIDONE

Introduction:

Furazolidone (FZD) is a synthetic nitrofurane derivative that is an antibacterial and antiprotozoal agent.¹ FZD occurs as a yellow odorless crystalline powder with a bitter aftertaste. The drug is practically insoluble in water and alcohol. FZD is decomposed by alkali. The drug should be protected by light because it darkens on exposure to strong light and thus should be stored in light resistant containers.¹

Uses & Indications:

FZD is active against the protozoan *Giardia lamblia* (*Giardia intestinalis*) and against a range of bacteria in vitro including staphylococci, enterococci, *Escherichia coli*, *Salmonella* spp., *Shigella* spp., and *Vibrio cholerae*.¹ FZD is bactericidal and appears to act by interfering with bacterial enzyme systems. Resistance is reported to be limited. It is used in the treatment of giardiasis, trichomoniasis, cholera and other vibrio infections.¹ It has been suggested for other bacterial gastrointestinal infections but antibacterial therapy with FZD is regarded as unnecessary in mild & self-limiting gastro-enteritis.¹ However, FZD has been reported to possess anti-*Helicobacter* activity² and to have some ulcer-healing properties.^{3,4,5}

Clinical experience has demonstrated that cure of *H.pylori* infection is difficult due to lack of compliance with drug regimens and development of antibiotic resistant *H.pylori*.⁶

FZD and nitrofurantoin have been recommended as alternative agents for the treatment of *H.pylori* due to the high rate of metronidazole resistance. When multiple treatment regimens fail, it has been suggested that salvage therapy regimens such as bismuth or FZD quadruple therapy should be used.⁷ In a recent study Kwon et al., (2000) assessed the prevalence of FZD, nitrofurantoin & metronidazole resistance among *H.pylori* strains in 431 clinical isolates. 52% were metronidazole resistant compared to 2% (7 of 431) with resistance to FZD & nitrofurantoin.⁸ All seven FZD and nitrofurantoin resistant isolates were also resistant to metronidazole.⁸

Dosage & Administration.

For the treatment of giardiasis and for the adjunctive treatment of cholera, the usual adult dosage of FZD is 100mg (or 1.25mg/kg) four times daily. Children 5 years of age or older may receive 17-25 mg four times daily. FZD dosage probably should not exceed 8.8 mg/kg daily because of the possibility of producing nausea and vomiting. Diarrhea usually responds to FZD therapy within 25 days. If satisfactory clinical response is not attained within 7 days, the manufacturer recommends that FZD be discontinued; however for the treatment of giardiasis most clinicians recommend 7-10 days of FZD therapy.¹

In the treatment of H.pylori infection, one-week triple therapy, consisting of tripotassium dicitrato bismuth (TDB), 240mg b.d., low-dose FZD (100mg b.d.) and clarithromycin (250mg b.d.) achieved high cure rate of H.pylori.⁹ Liu et al.¹⁰,(2000) reported that quadruple therapy with TDB 240mg b.d., FZD 100mg b.d., josamycin 1000mg b.d. and famotidine 20mg b.d. produced eradication rates (intention-to-treat/per protocol) of 90/95%, and duodenal ulcer healing rate of 94%. Mild side effects occurred in only 18% of those receiving therapy.¹⁰ In a study conducted in Brazil, forty H.pylori-positive patients with duodenal ulcer were randomized to receive 20mg omeprazole o.m. or b.d. for one month plus 500mg clarithromycin (b.d.) and 200mg FZD (b.d.) for one week. Three months after the end of the treatment the eradication rates were 90% by intention-to-treat analysis, and 97% by per protocol analysis.¹¹ Mild side effects were observed in 25 patients, none of who abandoned the protocol. No difference was observed between 20mg and 40mg omeprazole daily doses.¹¹

Mechanism of Action & Pharmacokinetics.

FZD is bactericidal due to its interference with several bacterial enzyme systems, possibly including prevention of acetylation of coenzyme A. FZD also acts as a monoamine oxidase (MAO) inhibitor.

Following oral administration, FZD is poorly absorbed and is inactivated in the intestine. About 5% of an oral dose of FZD is excreted in the urine as unchanged drug and metabolites, which may tint the urine brown. The concentration of FZD in milk has not been determined.

Cautions.

GI Effects

Nausea and vomiting are the most common adverse effects of oral FZD therapy; abdominal pain and diarrhea occasionally occur. These effects can be minimized or eliminated by reducing the dosage or discontinuing the drug.

Sensitivity Reactions

Hypersensitivity reactions to oral FZD occur in a small number of patients and generally subside with discontinuance of the drug. Hypersensitivity reactions include a fall in blood pressure, angioedema, fever, arthralgia, urticaria, and a vesicular or morbilliform rash. Erythema multiforme, pulmonary infiltration, and pulmonary eosinophilia also have been reported and may due to hypersensitivity.

Other Adverse Effects

Headache and malaise occur occasionally with oral furazolidone therapy and can be minimized or eliminated by reducing dosage or discontinuing the drug. Following oral furazolidone administration, hypoglycemia, agranulocytosis, and, in one patient, partial deafness and dizziness have also been reported. Rarely, some patients receiving oral furazolidone experience a disulfiram-like reaction to

alcohol. Polyneuritis and hemolytic anemia (in patients with glucose-6-phosphate dehydrogenase deficiency and in neonates) also have been reported rarely.

Precautions and Contraindications

Oral furazolidone may cause mild, reversible intravascular hemolysis in patients with a genetic deficiency of glucose-6-phosphate dehydrogenase. Such patients should be observed closely while receiving the drug, and furazolidone should be discontinued if any evidence of hemolysis occurs.

Although there have been no reports of adverse effects, the possibility of drug interactions characteristic of MAO inhibitors should be considered in patients receiving oral furazolidone, especially if the drug is administered in large doses or for prolonged periods. Because of a potential risk of hypertensive crisis, MAO inhibitors should be used with caution, if at all, in patients receiving indirectly acting sympathomimetic amines (e.g., amphetamines, cyclopentamin, dopamine, ephedrine, metaraminol, methylphenidate, phenylephrine, psuedoephedrine) or tyramine-containing foods (e.g. broad beans, yeast extracts, strong unpasteurised cheeses, beer, wine, pickled herring, chicken livers, and fermented products). MAO inhibitors should also be used cautiously, if at all, in patients receiving other MAO inhibitors, sedatives, antihistamines, tranquilizers, opiates, or chocolate.

Oral furazolidone is contraindicated in patients who have exhibited hypersensitivity to the drug.

Pediatric Precautions

Furazolidone should not be administered to infants younger than 1 month of age (who have immature enzyme systems and glutathione instability) because of the possibility of producing hemolytic anemia.

Carcinogenicity

Animal studies have demonstrated that oral furazolidone is tumorigenic when administered chronically.

Pregnancy, Fertility, and Lactation

Safe use of oral furazolidone in women who are or may become pregnant has not been established, but there have been no reports of adverse effects of the drug on the fetus or neonate. Use of furazolidone during pregnancy should be restricted to those cases where the possible benefits outweigh the potential risks.

Large oral doses of furazolidone appear to depress spermatogenesis by action on the seminiferous tubules, but usual doses reportedly do not have this effect.

Because of the concentration of furazolidone in milk has not been determined, safe use of oral furazolidone in nursing women has not been established.

Drug interactions:

Alcohol

Rarely, patients receiving oral furazolidone have exhibited a disulfiram-like reaction to alcohol characterized by flushing, slight temperature elevation, hypotension, dyspnea, and, in some cases, a sense of constriction in the chest. All symptoms reportedly disappear within 24 hours after ingestion of alcohol. If indicated, norepinephrine may be used to combat hypotensive episodes; indirectly acting pressor agents should be avoided. The mechanism of the interaction between furazolidone and alcohol has been postulated to be either inhibition of aldehyde dehydrogenase or inhibition of monoamine oxidase. It has been recommended that ingestion of alcohol in any form be avoided during oral furazolidone treatment and for 4 days thereafter to prevent this reaction.

Laboratory Test Interferences:

Tests for Urinary Glucose

Furazolidone metabolites present in the urine following oral administration of the drug may interfere with tests performed with cupric sulfate reagent (Benedict's Qualitative Regent, Clinitest®, Fehling's Solution, yielding false-positive results for urine glucose.

REFERENCES

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- ¹⁰ Liu W.Z., Xiao S.D., et al. A new quadruple therapy for *H. pylori* using tripotassium dicitrato bismuthate, furazolidone, josamycin and famotidine. *Aliment Pharmacol Ther* 2000; **14**: 1519-22.
- ¹¹ Dani R., Queiroz D.M. et al. Omeprazole, clarithromycin and furazolidone for the eradication of *H.pylori* in patients with duodenal ulcer. *Aliment Pharmacol Ther* 1999; **13**: 1647-52